

Docket No. 262905US0PCT

**MAIL STOP PCT****IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

IN RE APPLICATION OF: Pascale GAILLARD, et al.

SERIAL NO: 10/516,330 ✓

GAU:

FILED: December 14, 2004

EXAMINER:

FOR: AZOLE METHYLDENE CYANIDE DERIVATIVES AND THEIR USE AS PROTEIN KINASE MODULATORS

**INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR 1.97**

COMMISSIONER FOR PATENTS  
ALEXANDRIA, VIRGINIA 22313

SIR:

Applicant(s) wish to disclose the following information.

**REFERENCES**

- The applicant(s) wish to make of record the references listed on the attached form PTO-1449. Copies of the listed references are attached, where required, as are either statements of relevancy or any readily available English translations of pertinent portions of any non-English language references.
- A check or credit card payment form is attached in the amount required under 37 CFR §1.17(p).

**RELATED CASES**

- Attached is a list of applicant's pending application(s), published application(s) or issued patent(s) which may be related to the present application. In accordance with the waiver of 37 CFR 1.98 dated September 21, 2004, copies of the cited pending applications are not provided. Cited published and/or issued patents, if any, are listed on the attached PTO form 1449.
- A check or credit card payment form is attached in the amount required under 37 CFR §1.17(p).

**CERTIFICATION**

- Each item of information contained in this information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement.
- No item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned, having made reasonable inquiry, was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of this statement.

**DEPOSIT ACCOUNT**

- Please charge any additional fees for the papers being filed herewith and for which no check or credit card payment is enclosed herewith, or credit any overpayment to deposit account number 15-0030. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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Form PTO 1449 (Modified)  LIST OF REFERENCES CITED BY APPLICANT		ATTY DOCKET NO. 262905US0PCT		SERIAL NO. 10/516,330			
		APPLICANT Pascale GAILLARD, et al.					
		FILING DATE December 14, 2004		GROUP			
		FOREIGN PATENT DOCUMENTS					
		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION YES                  NO		
✓	AA	01/47920	07/05/01	WO			
	AB	00/35921	06/22/00	WO			
	AC	00/35909	06/22/00	WO			
	AD	00/35906	06/22/00	WO			
	AE	00/64872	11/02/00	WO			
	AF	1 110 957	06/27/01	EP			
	AG	02/20495	03/14/02	WO			
	AH	02/10141	02/07/02	WO			
	AI	02/22608	03/21/02	WO			
	AJ	0 169 502	01/29/86	EP			
OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)							
	AK	XIE, Xiaoling et al. "Crystal structure of JNK3: a kinase implicated in neuronal apoptosis", Structure, vol. 6, no. 8, pages 983-991 1998					
	AL	KUMAGAE, Yoshihiro et al. "Human c-Jun N-terminal kinase expression and activation in the nervous system", Molecular Brain Research, vol. 67, no. 1, pages 10-17 1999					
	AM	YANG, Derek D. et al. "Absence of excitotoxicity-induced apoptosis in the hippocampus of mice lacking the Jnk3 gene", Nature, vol. 389, pages 865-870 1997					
	AN	YANG, Derek D. et al. "Differentiation of CD4+ T Cells to Th1 Cells Requires MAP Kinase JNK2", Immunity, vol. 9, pages 575-585 1998					
	AO	SABAPATHY, Kanaga et al. "JNK2 is required for efficient T-cell activation and apoptosis but not for normal lymphocyte development", Current Biology, vol. 9, no. 3, pages 116-125 1999					
	AP	WOODGETT, James R. "A common denominator linking glycogen metabolism, nuclear oncogenes and development", TIBS, vol. 16, pages 177-181 1991					
	AQ	SAITO, Yuji et al. "The mechanism by which epidermal growth factor inhibits glycogen synthase kinase 3 in A431 cells", Biochem. J., vol. 303, pages 27-31 1994					
	AR	WELSH, Gavin I. et al. "Glycogen synthase kinase-3 is rapidly inactivated in response to insulin and phosphorylates eukaryotic initiation factor eIF-2B", Biochem. J., vol. 294, pages 625-629 1993					
	AS	CROSS, Darren A.E. et al. "The inhibition of glycogen synthase kinase-3 by insulin or insulin-like growth factor 1 in the rat skeletal muscle cell line L6 is blocked by wortmannin, but not by rapamycin: evidence that wortmannin blocks activation of the mitogen-activated protein kinase pathway in L6 cells between Ras and Raf", Biochem. J., vol. 303, pages 21-26 1994					
	AT	GRIMES, C.A. et al., Progress in Neurobiology, vol. 65, pages 393-426 2001					
	AU	KLEIN, Peter S. et al. "A molecular mechanism for the effect of lithium on development", Proc. Natl. Acad. Sci., vol. 93, pages 8455-8459 1996					
	AV	FLUECKIGER-ISLER, Rosina E. et al. "Stimulation of rat liver glycogen synthesis by the adenosine kinase inhibitor 5-iodotubercidin", Biochem. J., vol. 292, pages 85-91 1993		<input checked="" type="checkbox"/> Additional References sheet(s) attached			
Examiner			Date Considered				
*Examiner: Initial if reference is considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							

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				FILING DATE	GROUP
OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)					
•	AW	MASSILLON, Duna et al. "Identification of the glycogenic compound 5-iodotubercidin as a general protein kinase inhibitor", Biochem. J., vol. 299, pages 123-128 1994			
	AX	LOVESTONE, Simon et al. "Alzheimer's disease-like phosphorylation of the microtubule-associated protein tau by glycogen synthase kinase-3 in transfected mammalian cells", Current Biology, vol. 4, no.12, pages 1077-1086 1994			
	AY	BROWNLEES, Janet et al. "Tau phosphorylation in transgenic mice expressing glycogen synthase kinase-3beta transgenes", NeuroReport, vol. 8, pages 3251-3255 1997			
	AZ	STAMBOLIC, Vuk et al. "Lithium inhibits glycogen synthase kinase-3 activity and mimics Wingless signalling in intact cells", Current Biology, vol. 6, no. 12, pages 1664-1668 1996			
	AAA	CHEN, Guang et al. "The Mood-Stabilizing Agent Valproate Inhibits the Activity of Glycogen Synthase Kinase-3", Journal of Neurochemistry, vol. 72, pages 1327-1330 1999			
	AAB	TAKASHIMA, Akihiko et al. "Presenilin 1 associates with glycogen synthase kinase-3beta and its substrate tau", Proc. Natl. Acad. Sci., vol. 95, pages 9637-9641 1998			
	AAC	ZHANG, Zhuohua et al. "Destabilization of beta-catenin by mutations in presenilin-1 potentiates neuronal apoptosis", Nature, vol. 395, pages 698-702 1998			
	AAD	TAKASHIMA, Akihiko et al. "Tau protein kinase I is essential for amyloid beta-protein-induced neurotoxicity", Proc. Natl. Acad. Sci., vol. 90, pages 7789-7793 1993			
	AAE	PEI, Jin-Jing et al. "Distribution, Levels, and Activity of Glycogen Synthase Kinase-3 in the Alzheimer Disease Brain", Journal of Neuropathology and Experimental Neurology, vol. 56, no.1, pages 70-78 1997			
	AAF	NONAKA, Shigeyuki et al. "Chronic lithium treatment robustly protects neurons in the central nervous system against excitotoxicity by inhibiting N-methyl-D-aspartate receptor-mediated calcium influx", Proc. Natl. Acad. Sci., vol. 95, pages 2642-2647 1998			
	AAG	THOMAS, Robert Joseph. "Excitatory Amino Acids in Health and Disease", JAGS, vol. 43, pages 1279-1289 1995			
	AAH	SASAKI, Chihoko et al. "Different expression of glycogen synthase kinase-3beta between young and old rat brains after transient middle cerebral artery occlusion", Neurological Research, vol. 23, pages 588-592 2001			
	AAI	CROSS, Darren A.E. "Selective small-molecule inhibitors of glycogen synthase kinase-3 activity protect primary neurones from death", Journal of Neurochemistry, vol. 77, pages 94-102 2001			
	AAJ	ALI, Adnan et al. "Glycogen Synthase Kinase-3: Properties, Functions, and Regulation", American Chemical Society, pages A-N 2000			
	AAK	NAERUM, Lars et al. "Scaffold Hopping and Optimization towards Libraries of Glycogen Synthase Kinase-3 Inhibitors", Bioorganic & Medicinal Chemistry Letters, vol. 12, pages 1525-1528 2002			
	AAL	CHABAFA, Laila M. et al. "Facile Synthesis of 2-Furyl-, 2-Pyrrolyl-, 2-Imidazolyl- and Pyrrolo-Azoles from 2-Substituted Methylazoles", Polish J. Chem., vol. 68, pages 1317-1325 1994			
	AAM	ABDELHAMID, Abdou O. et al. "Reactions with Hydrazonoyl Halides. Part 10. Formation of Thiohydrazide, Hydrazonoyl Sulfide and Arylazothiazole Derivatives", J. Chem. Research (S), pages 144-145 1995			
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<b>FILING DATE</b> December 14, 2004		GROUP	
<b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>			
AAN	BROWN, Michael D. et al. "A New General Synthesis of 2-(N-Mono- and N-Di-substituted Amino)thiazoles", J. Chem. Soc. Perkin. Trans. I, vol. 52, no. 5, pages 1623-1626 1985		
AAO	DAWOOD, Kamal M. et al. "Polyheterocyclic ring systems with bridgehead nitrogen atoms: a facile route to some novel Azolo-1,2,4-triazine derivatives", J. Chem. Research (S), pages 206-207 2000		
AAP	GAUDRY, M. et al. "Enolisation des Cetones Dissymetriques-III", Tetrahedron, vol. 26, pages 5611-5615, with English abstract 1970		
AAQ	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290627, XP002218003 2002		
AAR	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290629, XP002218005 2002		
AAS	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290615. XP002218009 2002		
AAT	BLYUMIN, E.V. et al. "Reaction of 2-hetarylacetonitriles with ethyl 2-alkylsulfanyl-4-chloro-5-pyrimidinecarboxylates. Synthesis of new condensed pyrimidines", Tetrahedron, vol. 58, no. 28, pages 5733-5740, XP004369422 2002		
AAU	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2832472, XP002218001 2002		
AAV	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290610, XP002218002 2002		
AAW	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2833110, XP002218004 2002		
AAX	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290614, XP002218006 2002		
AAY	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2001:2009866, XP002218007 2002		
AAZ	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290631, XP002218008 2002		
BAA	"Exploratory Library (Catalog)", Ambinter, Chemical Abstracts Service, Database accession no. 2002:2290611, XP002218010 2002		
BAB	FISCHER, E. et al. "Cyclisierungsreaktionen von 1-[2-Amino-1-cyan-2-thio]-ethylene-pyridiniumbetainen", Journal f. prakt. Chemie, vol. 321, no. 3, pages 429-436, XP008009779, with English abstract 1979		
BAC			
BAD			
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#### STATEMENT OF RELEVANCY

- 1) References AA, AAQ-AAT have been cited in the International Search Report. Copies of these references are being submitted herewith only when not automatically provided by the International Searching Authority.
- 2) References AAU-BAB have been cited in the corresponding Partial European Search Report. A copy of these references is being submitted herewith.
- 3) References AB-AAP are discussed in the specification. A copy of these references is being submitted here with.
- 4) References \_\_\_\_\_ are additional prior art known to Applicant. A copy of these references is being submitted herewith.